OTITIS MEDIA AND ITS EXTENSIONS*

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THE title of this paper may seem strange to some. It is based on the consideration that mastoiditis, petrositis, labyrinthitis, Bezold's abscess, sinus thrombosis, and brain abscess, as well as meningitis of otic origin, are simply "extensions" of otitis media. The middle ear is the primary focus and also the most important drainage point, hence the emphasis will be on it rather than on other parts.

To understand the chemotherapy of otitis media and its extensions it is necessary to know something of the average course of the disease and something of the development and detailed anatomy of the temporal bone. As every physician knows, the latter consists of relatively flat outer parts called the squamous and mastoid portions from which projects inward a roughly three-sided structure called the petrous pyramid. This pyramid is the most important part of the temporal bone because it forms the keystone of the base of the skull and contains the middle ear and labyrinth. The labyrinth will not concern us in this paper because it is only secondarily involved in infections of the temporal bone. We are here only interested in the primary infections. As mentioned above, these spring almost invariably from the middle ear, although blood stream infections from distant foci have been described.

Simply stated, the external auditory meatus develops from the first branchial cleft, while the middle ear and Eustachian tube develop from the first branchial pouch. The lining of the middle ear cavity, therefore, is made up of mesoderm and entoderm which is continuous with mesoderm and entoderm of the nasopharynx. The ear drum is the partition between the outside and inside invagination and consists therefore, not only of the lining of the middle ear but also of the stratified squamous epithelium which develops from the ectoderm of the embryo. Now at birth, the middle-ear cavity is almost entirely filled with mesoderm, but

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as the individual grows this becomes thinner and thinner, so that in adults the submucosal tissues are so thin that they lie directly on the underlying bone. This single, rather flat-celled layer of epithelium and its underlying connective tissue is therefore often called "mucoperiosteum."

At birth the petrous pyramid, exclusive of the middle ear cavity, consists of bone, labyrinth, fibroblastic marrow and spaces for blood vessels. As the temporal bone grows, the fibroblastic marrow begins to be replaced by air-filled mucous membrane which pushes out in all directions, but most extensively through the antrum, into the mastoid and thence into the squamous portions of the bone.

Just how far this process will go in a given, growing child we have no means of prediction. In the opinion of the author, normal pneumatization of the temporal bone is largely a matter of the hereditary formation of the skull. Perhaps the size of the brain has something to do with it (cf. the studies of Dyke and Davidorf in cases of hemiatrophy of the brain). The generally accepted theory is that of Wittmaack who believes that reduced pneumatization is due to early infection of the mucous membrane which prevents normal invagination of the air-filled middle-ear sac. Others present different theories. Actually, we do not know any more about why some mastoids are large and highly pneumatized than we do about why some feet are big and flat while others are small and arched. There are undoubtedly many factors, some normal, some pathologic, which contribute to the final result. However, it makes a great difference whether the temporal bone is highly pneumatized or not. The great surface presented by many air cells lined with mucous membrane can excrete entirely too much fluid, if inflamed, to evacuate through the Eustachian tube or through a perforation in the drum membrane. Extension of the inflammation and pain due to the pressure are the result. Furthermore, if the temporal bone is extensively pneumatized, there is more chance for infection to become shut off at a distant point where drainage through the middle ear is impossible. It is these cases which often come to mastoid surgery or to surgery deeper in the temporal bone.

It must be remembered, to understand the foregoing discussion, that the middle ear is actually not a small cavity with specific dimensions as is intimated in most text books. Actually, it is almost impossible to measure the capacity of the middle ear because air cells in and around it

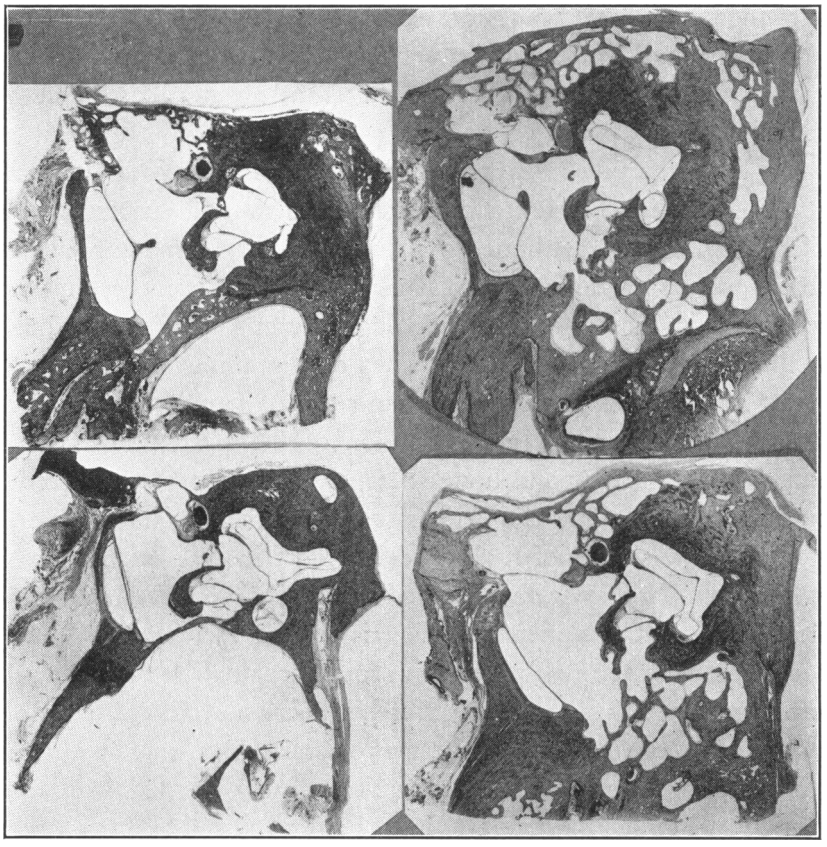

Fig. 1—Vertical section through four temporal bones at the depth of the round and oval windows showing the variation in the size of the middle ear cavity and the communication of the middle ear cavity with surrounding air cells.

vary so tremendously from case to case (Fig. 1). When the middle ear becomes infected, these air cells also become infected so that it is impossible to have otitis media without some mastoiditis, and if the petrosa is pneumatized, impossible to have otitis media without some petrositis. The air cells allow the infectious processes to involve at once a large part of the temporal bone. Their partitions are thin and are normally poorly vascularized, and worse than this, their connections are usually relatively small. It is really a wonder that infections of the mastoid so often get well without surgery. Furthermore, the air cells, especially in children, abut directly on bone marrow, and in certain types of infection, this becomes involved in the disease. It has not yet been ascertained

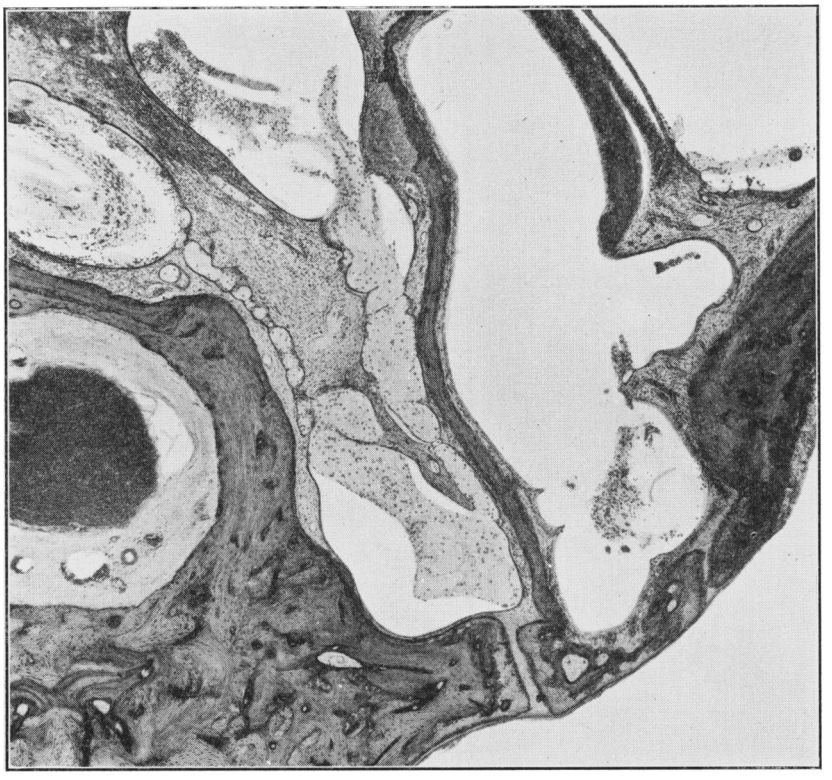

Fig. 2—Photomicrograph showing mild, low-grade inflammation in the niche of the oval window.

whether it is the increased vascularization and local leukocytosis of inflammation which permits the body to take care of such poorly drained areas, or whether it is a stifling of the growth of the invading organism by the production of anaerobic conditions. Conceivably all of these factors and perhaps more are responsible.

Mode of Infection in Otitis Media

The complicated series of cavities in the temporal bone can become infected in a number of ways. In infants, the most usual way is for the nasal secretions to run into the Eustachian tubes as the child lies on his back during an upper respiratory infection. Very small children cannot blow their noses or hawk mucus from their nasopharynxes, and since their Eustachian tubes are relatively short and straight, infection easily

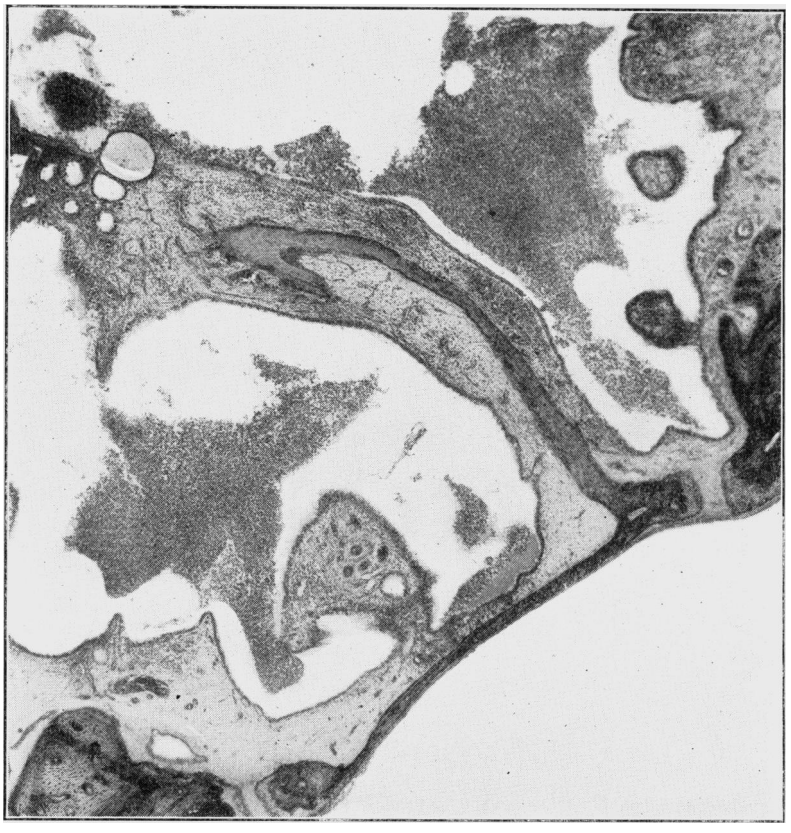

Fig. 3—More advanced stage of inflammation in the niche of the oval window. Note increased vascularization and thickness of the mucous membrane about the anterior crus of the stapes.

enters their middle ears. If they are turned on their bellies, however, it may easily drain out again. There is much less suppurative otitis media in the infant wards where babies are turned over regularly. With older children and with adults, the commonest method of infecting the middle ear seems to be from blowing the nose too violently. Marked sudden changes in pressure, such as those produced by deep diving may also suck infected material from the nasopharynx into the middle ear. Occasionally an ear drum becomes perforated or ruptured, permitting infection from the external canal to enter the middle ear, but even in these cases the usual cause of the infection is the nasopharynx. The perforation in the drum makes it very much easier to blow infected material

into the ear because there is no longer a closed cavity. How much infection of the middle ear takes place through the submucosa of the Eustachian tube due to its contiguity with the nasopharyngeal lining is still a matter of conjecture.

Pathology of Otitis Media

Regardless of how an infection enters the middle ear, the pathology is at first the same. There is edema of the mucous membrane, which swells five to ten times the normal thickness, then a serous effusion into the cavity. Following this there is a leukocytic infiltration of the submucosa beginning perivascularly and then extending to involve the entire mucoperiosteum. As time goes on, the effusion into the cavity tends to become purulent. At first, polymorphonuclears are quite prominent, but soon very few can be found among the monocytes. As fluid and sometimes gas collects in the cavity, the drum bulges outward and more and more of the surrounding cells become involved. The more virulent the infection in the submucosa, the more quickly the effusions become purulent, and the more reaction produced not only in the middle ear but also in the surrounding air spaces. If the infection is fulminating, the drum either ruptures spontaneously or has to be opened by a surgeon. Drainage is effected, and as a rule there is subsidence of the process in four to thirty days. Very mild processes, however, have been known to subside in twenty-four hours, but occasionally there is a smoldering infection which does not subside for several months. If the infection in the main cavity persists more than a few days, it almost invariably becomes more purulent, spreads and pockets in several places producing a thrombophlebitis of small veins in the mastoid and petrosa and thereby brings about necrosis of the air cell system. Excessive fluids secreted by the mucous membrane may also produce destruction of the bone by direct pressure. Microscopic sections show the mucoperiosteum of both middle ear and mastoid cells to be densely packed with leukocytes and fibroblasts. There is also destruction of the epithelium at various points and consequent invasion of the cavities with granulation tissue. With the breaking down of bone there is always some regrowth of osteoid, but in progressing empyema the regrowth of bone lags behind the breaking down. The cortex of the temporal bone may erode at any point, producing an abscess behind the auricle, over the lateral

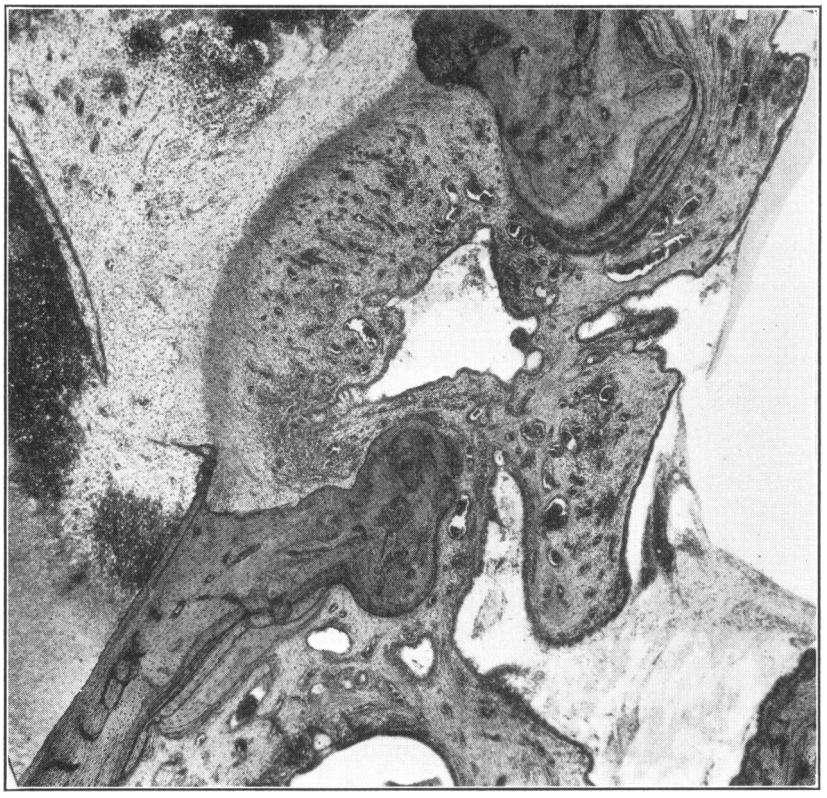

Fig. 4—Still more advanced inflammation in the region of the round window and beginning polypoid degeneration.

sinus, in one of the cranial fossae, or even in the neck, cheek, or nasopharynx. The more extensive the air spaces, the more chance of infected material becoming caught in some out of the way pocket and so producing a focus which will seek drainage by breaking through the cortex in this way. No matter how extensive the pneumatization, however, there is always some marrow in the temporal bone which is contiguous with the most peripheral air spaces. With infection of the air spaces there is always some reaction in this marrow, and occasionally, especially in young bones, the infection actually invades the marrow spaces, producing an osteomyelitis.

For purposes of simplification, then, the pathology of otitis media and its extensions can be divided into four distinct steps: first, edema of the mucoperiosteum and serous exudation; second, increased vascu-

larization of the submucosa, infiltration with leukocytes, proliferation of fibroblasts and increased purulency in the exudation; third, after two or three weeks, necrosis of the soft tissues as well as the bony walls of the cavity (this can now be seen in roentgenograms); fourth, especially if the process is less fulminating, there may develop polypoid degeneration of the mucoperiosteum and a prolonged, low-grade osteitis and osteomyelitis.

Any one of these four processes may stop, regress, and heal, leaving a more fibrotic mucous membrane and organized bands of scar tissue attached to the ossicles. Usually there is some reduction in size of the air cavities which already exist, and in young children infections may inhibit further pneumatization of the mastoid.

With repeated infections the processes are very similar in each instance except that inflammation in previously formed scar tissue produces much less vascularization than in normal tissue. The scar tissue may toughen the drum so that it does not break. Pressure then builds up in the middle ear and spreads the infection more deeply. Furthermore, with the regrowth of bone in the previous infections the connection between the mastoid cells as well as the antrum is likely to be narrowed. This increases the possibility of infection becoming trapped deep within the bone, and explains why complications most often occur in cases with a history of previous otitis media.

Therapy of Otitis Media

The treatment of otitis media for the last several decades has been directed towards the provision of adequate drainage for the middle ear and its surrounding air cells. If the infection was mild (so-called "acute-catarrhal" otitis media) drainage was usually obtained by reduction of infected material in the nose and by shrinkage of the Eustachian tube orifice. If the infection was more acute or more purulent, incision of the drum was resorted to. After myringotomy or spontaneous puncture the canal was simply kept clean to promote drainage either with dry wipes or irrigations of various kinds. If these did not suffice and the mastoid was seen to be breaking down in the roentgenogram, a mastoidectomy was performed, usually in the third or the fourth week of the infection.

Since 1936 the use of sulfanilamide and related drugs has been added to our resources. A great many cases show subsidence of symp-

TABLE I

FACTORS IN OTITIS MEDIA

1. Age: Infants and old people apparently more susceptible.
2. Sex: No essential difference.
3. Place: Flora and fauna vary in different vicinities.
4. Environment
5. Station in Life: Clinic patients seem to have more trouble than private patients.
6. Habits: Blowing of nose, swimming, etc.
7. Diet: Vitamins, etc.
8. Previous Infection and Immunity to Infection.
9. Mode of Infection
10. Time: Yearly cycles of incidence, March and April peak, etc.
11. General Physical Condition: Debilitating disease.
    Allergy.
12. Heredity: Race.
    Susceptibility to infection.
    Anatomy:
        Pneumatization of the temporal bone.
        Type of Eustachian tube.
        Lymphoid diathesis.
13. Skill of Physician and of Nursing.
14. Reaction to Surgery.
15. Reaction to Medication: Sensitivity.
    Tolerance:
        Vomiting.
        Excretion, etc.
    Individual Response.
16. Type of Infection.
17. *Chance.*

toms after chemotherapy so that many physicians have come to believe that it is the only treatment for otitis media, and are beginning to use it in every case. Even the lay public often asks that it be prescribed.

The bad results from improperly conducted chemotherapy often reach the hands of the otologist, so that he tends towards the opinion that drugs are of questionable value. Certainly the present ones mask symptomatology, sometimes cause unpleasant reactions, and make the problems of management harder for him. We have, then, on one side the general doctor and the pediatrician who tend to treat all types of otitis media (often even the non-suppurative types) with chemotherapy, and on the other the otologist who uses it only in desperate cases such as meningitis. Which is correct? Is there a middle ground? Is there some

rule which has scientific rationale, and which will work in the majority of cases? I believe that the rule can be built out of a study of the normal course of the disease, the pathology outlined above, and the results obtained in various types of cases by various methods of administration.

As already intimated, there are a great many factors which may influence the course of otitis media. These are summarized in Table I. Many have never been thoroughly studied, but a little thought about each one will tend to give it proper significance.

A word is perhaps necessary for certain items: under Heredity we have listed Anatomy, which is divided into pneumatization (already discussed) and Eustachian tubes, diameter, and curvature. Very little is known on this last subject except that certain people seem to have much more trouble with their tubes than others. It is also known that excessive lymphoid tissue about the tube seems to be an hereditary trait, and that this tissue tends to stop up the tubes and predispose to otitis media unless proper measures such as adenoidectomy or radiotherapy are used to combat it. Certainly the use of chemotherapy has not yet precluded the necessity for adenoidectomy in cases of recurrent otitis media.

It may surprise some to see a heading *Susceptibility to Infection* under Heredity. The work of Webster at the Rockefeller Institute, however, has definitely established this for mouse typhoid and mouse encephalitis, and the author has found hereditary susceptibility for otitis media in rats which could be bred out of a colony. There is no doubt that otitis media seems to run through certain human families.

Types of Infection

Table II shows that we have a specific chemotherapy for less than half of the total number of cases of otitis media. For over 35 per cent of the cases are due to the staphylococcus and more than 15 per cent are due to other organisms for which no specific chemotherapy has as yet been developed. However, about 30 per cent are due to the hemolytic streptococcus for which we have sulfanilamide, and 12 to 16 per cent are due to pneumococci for which we now have sulfapyridine. Study of Table III will show that three-quarters of the pneumococcus and streptococcus cases get well within three weeks without chemotherapy. These two tables indicate clearly that the group that needs to be treated with chemotherapy is definitely a small one.

TABLE II

PERCENTAGE OF VARIOUS ORGANISMS FOUND IN PURE CULTURE AT THE COLUMBIA PRESBYTERIAN MEDICAL CENTER IN THE YEARS 1933 TO 1939

Year	*Strep Hemo*	*Strep Other*	*Pneumo I*	*Pneumo III*	*Pneumo Other*	*Staph All Types*	*Others*
1933 273 cases	31.13	4.39	2.56	6.22	4.02	41.75	9.89
1934 334 cases	35.2	3.3	3.0	5.7	3.6	41.8	7.8
1935 333 cases	34.6	1.8	4.2	8.1	9.0	32.7	9.6
1936 336 cases	33.1	2.6	8.0	11.9	10.4	27.4	6.6
1937 517 cases	38.7	2.5	3.7	5.0	9.3	33.5	7.3
1938 524 cases	26.44	3.66	5.2	4.63	5.5	41.50	14.9
1939 438 cases	36.78	.91	4.1	5.51	6.4	36.78	10.11
Total 2,755 cases	33.6	2.7	4.45	6.4	7.04	36.7	9.5

TABLE III

DURATION OF DISCHARGE AND NUMBER OF PATIENTS THAT CAME TO MASTOIDECTOMY OUT OF 455 CASES DIAGNOSED AS OTITIS MEDIA, ACUTE SUPPURATIVE, IN THE COLUMBIA PRESBYTERIAN MEDICAL CENTER FROM MAY 1936 TO MAY 1937

	1-6 days	*7-14 days*	*15-21 days*	*3-4 weeks*	*More than 4 weeks*	*Mastoid-ectomy*
Staph 173 cases	26	62	18	27	33	7
Hemo Strep 163 cases	22	42	21	22	26	30
Pneumo 101 cases	16	28	20	12	12	13
Other Organisms 20 cases	4	9	1	4	0	2

In all fairness it must be pointed out, however, that there is a flaw in the above argument. It assumes that the culture reports are accurate. As a matter of fact, the figures are undoubtedly not exact, for unfortunately many of the cultures were taken using a swab without sterilization of the external auditory meatus. (Incidentally it has been shown by Page that throat cultures are often apt to pick up the offending

pathogen more accurately than a careless swabbing in the external canal.) However, the cultures described above were all made in suppurative cases, and if one adds to these the non-cultured cases, especially the non-suppurative cases, it is still fair to say that in the present state of our knowledge chemotherapy is indicated for only a small percentage of all the cases of otitis media.

How shall the surgeon discover this small percentage? Can it be determined with our present meager knowledge of the action of the drug and our knowledge of the pathology of otitis media? Lockwood and others have definitely shown that sulfanilamide is less efficient in necrotic lesions, and that the more the necrosis, the less the likelihood that the drug will be sufficiently bacteriostatic to permit the body to annihilate it. As has been pointed out above, very little necrosis—as a rule—occurs in otitis media and mastoiditis, until the second week of the disease. It would seem, therefore, that in simple otitis media one can wait a week or ten days after the onset using the old, simple, mechanical methods of treatment. Then if there is no improvement and the case looks as if it might go on to surgical mastoiditis or a long siege of drainage, the administration of drugs may be begun with every expectation that they will stop the process if given in sufficient dosage. At the end of a week adequate bacteriological and blood studies should be available so that the correct drug can be selected. Analysis of cases treated with sulfanilamide (Table IV) shows that a large percentage of cases treated with adequate dosage, especially those in hospital, get well while those treated with small or short dosage in the clinic show no more tendency

TABLE IV

APPARENT EFFECT OF SULFANILAMIDE IN OTITIS MEDIA IN 100 UNSELECTED CASES

100 CASES	
Postoperative, questionable effect	6
Reaction	6
Recurrent	11

	Inadequate dosage	*Adequate dosage*
No effect	31	11
Questionable effect	18	3
Good effect	18	25

All but four of the cases on adequate dosage were in the hospital. "Questionable effect" represents cessation in less than two weeks. "Good effect" represents cessation of discharge in less than a week.

to recover than an untreated series (cf. Tables III and IV). The cases in which the drug has no effect are usually cases of inadequate dosage. Often there is recurrence if adequate dosage is not prolonged well after temperature is normal and drainage has stopped. If the drug is started late in the disease it may have no appreciable effect. Apparently the drug has less effect in cases where there has been a previous infection.

We have much divergence of opinion as to the dangers of chemotherapy. Many say that there is virtually no danger, especially in children, and that all drug-sensitive individuals show up on small dosage so that they can be spotted before any serious harm has been done. Others emphasize the danger of damage to the kidneys and liver; cite the patients who have died with anemia and leukocytopenia, or speculate on the effect of the drug on the reticulo-endothelial system in the years to come.

The physician must decide at the end of a week or ten days whether his case is going on to a surgical mastoiditis or is going to prolong itself enough so that the patient is in danger of acquiring a residual deafness. If he is fairly certain of one of these things, the dangers outlined above need hardly be considered. Chemotherapy should be instituted as a major procedure, comparable in every way to surgical interference. If possible, the patient should be hospitalized, and if not, careful blood and urine studies should be done every two days at home. The dosage should be fairly large (Long and Bliss suggest at least 2 mg. per kilo of body weight) and kept up for several days after the temperature has come to normal and the discharge behind the drum has ceased. If this is not done there will be almost certainly a recurrence of the disease, especially when the original organism is a virulent one.

Analysis of successful sulfanilamide-treated cases shows a dramatic subsidence of symptoms within three or four days. Most of them have no pain or fever after two days. This suggests that if there is no effect within three or four days the drug is not the answer, and that drainage will have to be instituted by one of the well-known surgical methods. In advanced or neglected cases surgery is usually essential, but of course may be supplemented by chemotherapy. After all, it is impossible to drain every nook and cranny in the temporal bone, and the chemotherapy will produce bacteriostasis in these unreachable regions. The combined use of surgery and chemotherapy is especially important in the complications of otitis media such as meningitis, brain abscess, and

inflammation of the walls of the venous channels draining the temporal bone.

To recapitulate, given a case of otitis media, chemotherapy should be instigated a week or ten days after the onset of the disease, if the patient does not seem to be getting well without it and a specific drug is available to combat the bacteria of the infection. The chemotherapy must be given in adequate dosage for a considerable period after symptoms begin to disappear and under careful surveillance of reactions and with surgical adjuncts to the therapy in mind. In no case should it be given casually, without cultures and without a knowledge that most otitis media is self-limiting. It must be remembered that the use of bacteriostatic drugs makes the management of the cases harder because the symptomatology of the disease processes is masked.

Some day it is hoped that we will have new drugs for all types of infection, and drugs which can be given without untoward outside effects—then of course, the above working rule for our present drugs will have to be modified.